REMARKS

Claims 12-18, 20-22, and 32 are pending in the present application.

Applicants gratefully acknowledge withdrawal of the rejection of claims 12-17 under 35 U.S.C. §102(e) from the prior Office Action.

Rejections under 35 U.S.C. §112, Second Paragraph.

Claims 12-18, 20-22, and 32 stand rejected under 35 U.S.C. §112, second paragraph as allegedly being vague and indefinite due to the recitation of the phrase "the composition being capable of preserving thyroid stimulating hormone present in the blood sample for at least about three weeks at an ambient temperature of about 22 °C" in claim 12. This rejection is unwarranted. According to the Office Action, in the paragraph bridging pages 2 and 3, this phrase renders the claims indefinite because it "fails to define an upper limit capacity for the composition to be able to preserve", is not "defined or supported" in the specification, and "reads on a capacity of preserving for about 10 years."

As noted in the MPEP, section 2173.02, the test for indefiniteness under the second paragraph of 35 U.S.C. 112 is whether those skilled in the art would understand what is claimed when the claim is read in light of the specification. Open ended numerical ranges are not *per se* indefinite (see MPEP 2173.05(c), subsection II.). The recited phrase in claim 12 is not indefinite, since one of ordinary skill in the art, in reading both the claim and the specification, would recognize that a statement of the ability to *preserve* a composition for a period of time is properly and adequately defined by reciting a minimum time period, so that it does not read on "zero" (i.e., no preservation). In contrast, stating an upper limit is unnecessary to define the invention. As the specification points out (e.g., in the Examples) the capability of the compositions to preserve TSH is determined by storing a TSH-containing blood sample in a composition of the invention and measuring the amount of TSH still present in the sample over a fixed period of time. If no significant degradation of TSH is observed during the test period, the only technically accurate statement that can be made about the TSH preservation capability of the composition is that it will preserve TSH for *at least the duration* of the test. One cannot expect Applicants to continue testing compositons, perhaps for years, just to come up with an upper limit on preservation capacity. An upper limit is not necessary or important for defining the invention. What is important is that the compositions preserve

TSH in the sample for long enough to allow for transport to a testing laboratory for analysis. The sample must be preserved at a sufficient level to allow the necessary clinical tests to be reproducibly performed on the blood sample preserved in the composition. The upper limit, beyond this, is irrelevant to the purpose and use of the claimed compositions. As is clear from the Example, preservation capability is temperature dependent. At lower temperatures, samples remain stable for longer periods of time. Once a sample arrives at a testing laboratory, it would be stored at well below ambient room temperature (e.g., in a refrigerator) prior to testing. One of ordinary skill in the art would clearly understand that it is the minimum time period of preservation capacity that is important based on the description of the tests in the specification. The minimum time period specified in the claim is readily determinable by the routine testing protocols described in the Examples. Thus, one of ordinary skill in the art would be able to determine what, precisely, is claimed in the application.

With regard to the issue of claim breadth, the MPEP clearly points out that breadth of a claim is not to be equated with indefiniteness (see MPEP 2173.04 on this specific point). Even if an upper limit for TSH preservation capacity were to have been stated (i.e., "is capable of preserving TSH in the sample for a period of between 3 weeks and 1 year), such a range would still read on preservation for 10 years. As noted above, the standard for definiteness is what one of ordinary skill in the art would understand from the language of the claim read in light of the specification. Here, a numerical minimum limit on the time period defining a preservation capability adequately and clearly describes the this feature of the claimed compositions, particularly in light of the description in the specification of how such capability is measured. Accordingly, this rejection should be withdrawn.

Rejections under 35 U.S.C. §112, First Paragraph.

Claims 12-18, 20-22, and 32 also stand rejected under 35 U.S.C. §112, first paragraph as allegedly lacking adequate written description in the specification. The Office Action, on page 3, indicates that the specification does not provide any "literal or descriptive support" for the phrase "the composition being capable of preserving thyroid stimulating hormone present in the blood sample for at least about three weeks at an ambient temperature of about 22 °C". Page 4 of the Office Action further goes on to state that "Recitation of claim

limitation lacking literal support in the specification or originally filed claims constitutes new matter." This is simply an incorrect statement of the law. The standard for the written description requirement is whether the disclosure in the application conveys "with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and the invention, in that context, is whatever is now claimed." See MPEP 2163.02 for a discussion of this standard. Literal support for a claim amendment is not required. *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). In this case, Applicants pointed to support in the Examples, which demonstrate preservation of TSH in a blood sample for the entire 3 week duration of the test at ambient room temperature. Applicants also provided a specific citation to page 7, lines 22-25, which does, in fact, *literally* support the claim language. In the Office Action, this passage is mis-stated by insertion of the words "up to" in square brackets before the words "at least about 3 weeks" in the quoted passage. The cited passage of the specification states, without added words:

> "The biological fluid preserving compositions of the present invention can preserve a specimen of a biological fluid, such as a whole blood specimen, when stored for up to about one week at a temperature of about 45 °C, and at least about 3 weeks at ambient room temperature or below." (emphasis added)

Two separate sets of test results are described in the quoted passage of the specification cited as support for the claim limitation. One set of tests was run at 45 °C, whereas a different set of tests was run at ambient room temperature (22 °C in this case). The words "up to" do not appear before "at least about" in the underlined passage describing the room temperature tests. Reading those words into the cited passage is unwarranted and unnecessary to define or understand the claimed invention. The Examples support the "at least about 3 weeks" limitation, as well, since three weeks was the entire duration of the room temperature tests, and no significant degradation of TSH was observed in any of the tested blood samples preserved by compositions of the invention in the ambient room temperature tests. As noted above, the manner in which the tests are run (i.e., for a fixed period of time) justifies the "at least about" wording in the limitation. Applicants fail to see what more

support is needed for the recited claim limitation. This rejection is based on an improper standard for the written description requirement, and should be withdrawn.

Rejections under 35 U.S.C. §103(a).

Claims 12-18, 20-22, and 32 also stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,579,688 (Steaffens *et al.*) in view of U.S. Patent No. 5,616,460 (Figard). This rejection is clearly unwarranted, as well. A *prima facie* case for obviousness requires that the references themselves must contain some teaching, suggestion, or motivation to combine their teachings. *In re Bell*, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993); *In re Fine*, 5 USPQ2d 1596, 1598 (Fed, Cir. 1988). Moreover, an obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to due reasonably skilled in the art. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Neither prong of this analysis has been satisfied in this instance. Furthermore, a *prima facie* case for obviousness requires that all claim limitations be taught or suggested by the prior art. *In re Royka*, 180 USPQ 580 (CCPA 1974). All words in a claim must be considered in judging the patentability of that claim against the prior art. *In re Wilson*, 165 USPQ at 496. The instant rejection falls short of these requirements.

Steaffens *et al.* is directed to a reagent for stabilizing polypeptides and antigens used in analytical procedures. The entire focus of Steaffens *et al.* is on preserving compositions that contain a serum (e.g., bovine serum albumin or fetal calf serum) and a detergent as key, active ingredients. The Office Action cites col. 3, lines 55-64 from the summary of the invention as support for the rejection. this cited passage is merely a generic list of components that *could* be present in the stabilizing composition:

> "In certain preferred embodiments, the reagent comprises one or more of the following: buffer(s), blocking agent(s), solvent(s), salt(s), chelator(s), detergents(s), and preservative(s)."

The cited section at col. 4, line 33 to col. 5, line 6 simply defines each of the components recited at col. 3, lines 55-64. In contrast to these general description, however, the specific teaching of Steaffens *et al.* is that a serum compound and a detergent are important, as active ingredients, to achieve suitable preservation of antigens and polypeptides. The entire summary of the invention of this patentis so general in nature that there is no

specific teaching of what components contribute to the alleged preservative activity of the purported invention. In fact, the only teaching of the purported improved preserving compositions in Steaffens *et al.* is found in the detailed description, beginning at col. 8, line 30. It is only from this point in the reference that one of ordinary skill in the art could determine just what specific components in the compositions are purportedly necessary to achieve the requisite preservation activity. All of the compositions described as being part of the purported invention of Steaffens *et al.* include, *inter alia*, a serum, such as fetal calf serum (FCS) or bovine serum albumin (BSA), as well as a detergent. All of the claims also require the presence of a serum and a detergent in the compositions. The reference teaches, at col. 9, lines 15-30, the importance and significance of the serum material and the detergent as active participants in the purported preserving activity of the compositions. It is clear from this passage that Steaffens *et al.* teach that the serum and detergent are key ingredients of the preservative compositions.

Frigard, on the other hand, teaches an entirely different type of composition than Steaffens *et al.*, i.e., a buffer composition containing dithiothreitol (DTT) and ethylene glycol as the active buffering components (see, e.g., the abstract; as well as the description at col. 2, line 40 through col. 3, line 2; col. 3, lines 15-21, and col. 4, line 33-67). The purpose of the DTT is described as preventing oxidation of sulfhydryl groups in a protein (see col. 4, lines 33-52), while the purpose of the ethylene glycol is described as preventing oxidation of the DTT (see col. 4, lines 53-67).

Each of claims 12-18, 20-22, and 32 includes all of the limitations of claim 12, which is directed to a composition suitable for lysing and preserving a blood sample for hormone analysis. The composition of claim 12 *consists essentially of* specified amounts of a chelating agent, a cell lysing agent, a preservative, and an antifreeze agent, in water. Furthermore, the composition is capable of preserving thyroid stimulating hormone (TSH) present in a blood sample for at least about 3 weeks at an ambient temperature of about 22 °C. As presently defined, the claims exclude other active ingredients, due to the relatively closed "consisting essentially of" language of the claims.

The applied references merely contain isolated, *general* disclosures of the various classes of compounds specified by the claims. Notably, the references do not teach or

suggest the combined specific amounts of chelating agent, cell lysing agent, preservative or antifreeze agent set forth in the present claims. The references themselves do not contain any motivation for one of ordinary skill in the art to have combined the isolated teachings of the references to obtain the *specific compositions* of the present claims. The fact that the Examiner has done so is evidence of impermissible hindsight reconstruction of the claimed invention using Applicants' own specification as a guide. The specific teachings Steaffens *et al.* and Frigard, on the other hand, actually teach away from the presently claimed invention.

The cited references specifically teach the importance of "serum" materials and detergents (Steaffens *et al.*) for preserving antigens and polypeptides, and the use of a combination of DTT and ethylene glycol to protect sulfhydryl groups in proteins from being oxidized. There is no teaching or suggestion in any of the cited prior art references, either alone, or in combination, that "serum" compounds (e.g., BSA or FCA) or DTT are within the scope of the present claims (i.e., chelating agents, cell lysing agents, preservatives, or antifreeze agents). Furthermore, the combined references do not teach or even suggest a composition that is capable of preserving thyroid stimulating hormone (TSH) in a blood sample for at least about 3 weeks at an ambient temperature of about 22 °C. Certainly there is no teaching or suggestion that would have provided one of ordinary skill in the art with a reasonable expectation of success at preserving TSH in a blood sample for at least about 3 weeks, since, as noted previously, the references are silent with respect to TSH stability.

In response to the arguments previously presented by Applicants, the Office Action states, on page 10, that the preservation capability limitation of the claims does not set out a structural limitation for the claimed compositions. This statement misses the point that the structural limitations of the claims are set forth in the lettered elements "a" through "d" in claim 12. The combined teachings of the applied references merely provide isolated, general descriptions of some materials within the broad description of the elements of the claims, but do not provide a motivation to combine these disparate elements in the manner set forth in the claims, to achieve the requisite TSH preservation activity.

At best, the combination of Steaffens *et al.* and Frigard would have suggested a preservative composition comprising a *combination* of a serum compound, a detergent, DTT, *and* ethylene glycol. While some detergents may be cell lysing agents, and ethylene glycol is

a known antifreeze, the present claims exclude the presence of an active amount of a serum compound or of DTT due to the "consisting essentially of" language. Thus, the combined references cannot render the present claims obvious, since the teachings of the references and the limitations of the present claims are mutually exclusive of one another. In other words, the cited references teach away from compositions of the present claims, since the claims exclude some of the very materials that are essential components in the compositions of the references (e.g., serum materials and DTT).

Accordingly, the present claims are patentable over the combined, applied references, since the combined references do not teach or suggest a composition having the structural or activity limitations set forth in the claims.

Conclusion.

All of the present claims are meet the requirements of 35 U.S.C. §112 and are patentable over the applied combination of prior art references. Accordingly, Applicants request reconsideration, withdrawal of finality, and early passage of the application to issuance.

Respectfully submitted,

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